## REMARKS

Claims 21-67 are active in the present application. Support Claims 45-66 is found in Claims 1-20 and the specification as originally filed. In addition, Applicants submit herewith a substitute Sequence Listing to clarify the sequences disclosed in the present application. Applicants further submit a corresponding computer-readable Sequence Listing. The sequence information recorded in the corresponding computer-readable Sequence Listing is identical to the paper copy of the substitute Sequence Listing. Support for all of the sequences listed in the substitute Sequence Listing is found in the present application as originally filed. The specification has also been amended to provide sequence identifiers (SEQ ID NO:). No new matter is believed to have been added by the submission of the substitute Sequence Listing and Claims 45-67.

Applicants wish to thank Examiner Brown for indicating that the subject matter of Claim 14 is free of the prior art, it is noted that the subject matter of Claim 14 is now presented in new Claim 59. In view of the amendments submitted herein and the following remarks, favorable reconsideration and allowance of all pending claims is requested.

Applicants affirm the election of Group I, Claims 1-20, with traverse.

As requested by the Examiner Applicants submit herewith copies of the Baccala and Sakano references. In addition, Applicants provide copies of the foreign patent documents, which the Examiner indicated had not been received. Accordingly, an indication that the Examiner has considered these references is requested.

The rejection of Claims 1-5 and 20 under 35 U.S.C. §102(e) over George et al (U.S. Patent 5,861,156) and Kamireddy et al (U.S. Patent 5,597,573) is obviated by the cancellation of these claims.

Claims 21-67 are not anticipated by George et al and Kamireddy et al for the following reasons.

George et al disclose methods of delivering agents to target cells using mono-specific binding proteins to label target cells to which specific agents can be delivered. George et al further disclose that a mono-specific binding protein includes binding protein fragments such as a single chain Fv (sFv) protein (see column 2, lines 61-66). This mono-specific protein is selected to bind to specific target cells and to multivalent antibodies carrying an agent or an effector cell which should be targeted to the cells. George et al further disclose that this binding protein binds to "one or more naturally-occurring cell surface markers, and thus, "modifies" the target cell" (see column 3, lines 46-49). This mono-specific binding protein also contains a tag that is recognized by a multivalent antibody, which can be heterospecific to a peptide tag and to an agent to be delivered to the target cell (see column 3, lines 26-28).

The George et al polypeptides are designed to modify target cells so that the target cells can be recognized by a multivalent antibody thereby targeting a specific agent to the surface of or in the proximity of the surface of the cell. Therefore, the mode of delivery in George et al is to target the agent to a specific cell, and particularly to the **cell surface** and as such provide no disclosure for polypeptides that **penetrate into a cell** as claimed.

Kamireddy et al disclose specific compounds that can stimulate the production of catalytic antibodies, which in turn, cleave lipopolysaccharides (LPS), particularly for the treatment of bacterial infections and septicemia (see column 1, lines 32-51). Kamireddy et al further disclose that "catalytic antibodies can have better penetration of **tissues** as catalytic antibodies can be IgG-type antibodies or catalytically active fragments thereof" ( column 4, lines 31-34, emphasis added). Therefore, the Kamireddy et al compound target tissues or

extracellular spaces (outside the cell) but do not disclose a polypeptide which can penetrate into cell as presently claimed.

In view of the foregoing George et al and Kamireddy et al do not anticipate the claimed invention and as such withdrawal of this ground of rejection is requested.

The rejection of Claims 1-5 and 20 under 35 U.S.C. §103(a) over George et al in view of Kamireddy et al and Curiel et al (U.S. Patent No. 5,521,291) is obviated by the cancellation of the claims.

The active claims in this application are not obvious in view of the combination of these references for the following reasons.

The deficiencies of George et al and Kamireddy et al with respect to the present claims are discussed at length above. Furthermore, with respect to the teachings in George et al, it is clear that the skilled artisan would avoid selecting fragments which penetrate **into** a cell because in so selecting such fragments, the skilled artisan would defeat the core purpose of George et al, i.e., targeting the cell surface of the cell with specific agents. Likewise, Applicants point out that Kamireddy et al teach that to obtain an efficient therapeutic effect, the compounds must reach the infection site where the bacteria are located. To this end, Kamireddy et al teaches: "bacteremia is a severe infection of microorganisms in the blood stream" (column 1, lines 65-66). Therefore, the compounds which are disclosed in Kamireddy et al target tissues, the blood-stream, or extracelluar spaces, but because the bacteria are not located in the cells, there is no need for compounds or polypeptides that penetrate into a cell. If the skilled artisan were to select compounds that penetrated into the cells, the primary purpose of the Kamireddy et al disclosure would also be lost.

Therefore, the skilled artisan would not have been motivated to modify the teachings of either George et al or Kamireddy et al to arrive at the present invention, because in so

doing the George and Kamireddy purposes would be lost. See MPEP §2141.03 "prior art must be considered in its entirety, including disclosures that teach away from the claim" and MPEP § 2143.01 "the proposed modification cannot render the prior art unsatisfactory for its intended purpose."

Notwithstanding this lack of motivation to modify the teachings of George and Kamireddy the Examiner relies on Curiel et al to teach conjugates of virus and antibodies to transport gene contracts into eukaryotic cells (referring to page 9 of the Official Action). The Examiner alleges that "one would have been motivated to modify the polypeptide of George et al to incorporate a polylysine region for additional internalizing potential because Curiel et al teach that the polylysine region has affinity for nucleic acid and is useful for directing their virus-conjugated-antibody into cells" and further that the skilled artisan would be motivated to screen for peptides in George using the methods known in the art (as evidenced by Kamireddy) that are able to penetrate into the cells (referring to the discussion on page 9 of the Official Action). However, for the reasons set forth above, the skilled artisan would not have been motivated to modify the teachings of George to identify polypeptides which penetrate into cells, because in so modifying George, the core principle of the George invention would be lost. Furthermore, even if the skilled artisan would have been motivated to screen for various compounds or polypeptides, there is no suggestion in any of the references that the skilled artisan would have any success in identifying a polypeptide with a cell penetration activity as claimed.

In the absence of a motivation to modify the teachings of the references or a suggestion for obtaining the claimed polypeptides, the combined teachings of the cited references cannot render the present claims obvious.

Withdrawal of this ground of rejection is respectfully requested.

The formal drawings were filed on January 31, 2002.

Applicants submit herewith a Abstract of the Disclosure in compliance with 37 C.F.R. §1.72(b).

The objection to Claims 6-15, 18 and 19 is obviated by amendment.

The rejection of Claims 1-5, 14, 16, 17 and 20 under 35 U.S.C. §101 is obviated by amendment.

The rejection of Claims 1-5, 14, 16, 17 and 20 under 35 U.S.C. §112, second paragraph is obviated by amendment.

Applicants submit that the present application is now in condition for allowance.

Early notification of such allowance is earnestly solicited.

Respectfully submitted,

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IN THE SPECIFICATION

Please amend the specification as follows:

Page 37, lines 15-19, replace the text in its entirety with the following:

In sequences 1 to 3 above, MDYWGQGT = Met-Asp-Tyr-Trp-Gly-Gln-Gly-Thr (amino acids 11-18 of SEQ ID NO:16) and FAYWGQGT = Phe-Ala-Tyr=Trp=Gly-Gln-Gly-Gly-Thr (amino acids 11-8 of SEQ ID NO:18). Further, the formula $(a\text{-}b\text{-}c)_m$ means that a single, some or all of the residues mentioned in brackets are present or not present.

Page 48, lines 21-22, replace the text in its entirety with the following:

$(K)_{19}$-V-A-Y-I-S-R-G-G-G-I-F-Y-Y-Q-D-S-I-K-G-R-F-T-R-E-K-Y-G-K-R-G-M-D-Y (SEQ ID NO:36);

Page 63, after the last line, beginning on a new page, please insert the Abstract of the Disclosure appended hereto.

After the Abstract of the Disclosure, please replace the Sequence Listing filed on May 18, 2001 and with the attached substitute Sequence Listing.

IN THE CLAIMS

Claims 1-20 (Canceled).

Claims 45-67 (New).